IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

William J. Curatolo et al.

Application No. 09/770,562

Filed: January 26, 2001

Confirmation No. 8513

For: SOLID PHARMACEUTICAL DISPERSIONS WITH ENHANCED BIOAVAILABILITY

Examiner: Blessing M. Fubara

Art Unit: 1613

Attorney Reference No. 8191-87018-01

FILED VIA EFS
ON 4/25/2012

FILED VIA ELECTRONIC FILING SYSTEM
BOARD OF PATENT APPEALS AND INTERFERENCES
UNITED STATES PATENT AND TRADEMARK OFFICE

APPEAL BRIEF

This is an Appeal Brief filed under 37 C.F.R. § 41.37. A Notice of Appeal was received by the U.S. Patent and Trademark Office (USPTO) on January 25, 2012, making the Appeal Brief due on or before April 25, 2012, with a one-month extension of time to file a brief. In accordance with 37 C.F.R. § 41.20(b)(2), this Appeal Brief is being filed together with the required fee of $620.00. Appellant also petitions for a one-month extension of time and submits the requisite fee of $150.00 herewith. If an additional extension of time is required, please consider this a petition therefor.

Please charge any additional fees that may be required in connection with filing this Appeal Brief including any extension of time or excess page charges to Deposit Account No. 02-4550.

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I. REAL PARTY IN INTEREST

The real party in interest is Bend Research, Inc., the assignee of record of the present application (Reel 21998, Frames 880-888, recorded on December 19, 2008).

II. RELATED APPEALS AND INTERFERENCES

Prior Appeal before the Board of Patent Appeals and Interferences, Appeal No. 2010-009640; Decision issued March 29, 2011 (Evidence Appendix 1).

III. SUMMARY OF CLAIMED SUBJECT MATTER

This application, having a priority date of August 11, 1997, concerns the invention of a spray-dried solid dispersion consisting of an amorphous drug molecularly dispersed in HPMCAS, and was developed more than 15 years ago at the very infancy of spray-drying technology for pharmaceuticals. Low solubility drugs are known to have poor bioavailability and/or irregular absorption. To address this problem the inventors developed this spray-dried solid dispersion of the drug in the amorphous state in hydroxypropyl methylcellulose acetate succinate (HPMCAS).

Specifically, **claim 1** recites

a spray dried solid dispersion *(p. 11, lines 9-22; p. 15, line 16 – p. 18, line 31)* consisting of:

a sparingly water-soluble drug *(p. 4, lines 29-31 and p. 7, lines 16-23)* and HPMCAS *(p. 10, lines 13-30)*,

the drug being molecularly dispersed *(p. 7, lines 26-28)* and amorphous in the dispersion *(p. 7, line 29-31)*,

having a drug:polymer weight ratio between 1:0.4 and 1:20 *(p. 13, lines 24-29)*, and

the dispersion is a homogeneous solid solution of said drug in said HPMCAS *(p. 16, lines 6-13; p. 12, lines 5-9)*.

VI. ARGUMENT

A. **Summary**: It is Appellant's position that no anticipation case or *prima facie* case of obviousness have been presented against the claims as the art cited by the Examiner fails to meet all of the claim limitations. The claim language includes the recitation "consisting of" an amorphous drug – that is, no crystalline drug in the spray-dried solid dispersion. None of the references, explicitly or inherently, discloses a composition *consisting of* an amorphous drug (i.e., not a crystalline drug) molecularly dispersed in a spray-dried solid HPMCAS/drug

dispersion. Further, none of the references are enabled such that the skilled artisan reading these references could make a composition *consisting of* amorphous drug molecularly dispersed in a spray-dried HPMCAS/drug solid dispersion.

The crux of the disagreements between the Examiner and Appellant are that:

1. the interpretation of the "consists of" language in claim 1 limits the dispersion claimed to only amorphous drug – that is, the dispersion does not include crystalline drug;
2. spray-drying does not inherently produce the claimed amorphous drug molecularly dispersed in a solid dispersion but instead may produce crystalline drug or a mixture of amorphous and crystalline drug; and
3. the cited prior art did not enable one of ordinary skill in the art (in 1997) to make a solid dispersion consisting of an amorphous (non-crystalline) drug molecularly dispersed in the HPMCAS/drug dispersion.

Notably, in rejecting the Appellant's arguments as to points 2 and 3, the Examiner appears to give no weight to the § 1.132 Declaration of Ann Newman (Ev. App. 2) presenting evidence that a spray-drying process does not necessarily result in a substantially amorphous solid dispersion as well as ignoring the § 1.132 Declaration of Ron Beyerinck (Ev. App. 3) presenting evidence that the cited references were not enabled for making the claimed spray-dried solid dispersions. The Appellant filed the evidence in these two Declarations after the Board indicated in the last appeal that such evidence was needed to support the assertion of non-enablement of the prior art, yet this evidence is all but ignored with the Examiner's wholly unsupported statement that the Declarations are not persuasive "because spray drying is a known technique and what is well known in the art does not have to be taught in the art." (Advisory Action dated 12/22/2011; Ev. App. 4.) However, at no time has the Examiner provided any evidence that such technique (to make an all amorphous (non-crystalline) drug molecularly dispersed in a spray-dried solid HPMCAS/drug dispersion) was well known in 1997. Furthermore, the Examiner does not comment on or in any manner acknowledge the evidence provided in the Declarations, which evidence shows that little if anything was known in 1997 as to these techniques and includes articles dated before 1997 showing both a lack of inherency as to producing spray-dry solid dispersion *consisting of* amorphous solid dispersions and a lack of enablement for spray drying the same.

B. The Cited Prior Art

Miyajima discloses a pharmaceutical composition comprising a solvate of the drug NZ-105 and HPMCAS. The patent makes no statement as to whether the drug is molecularly dispersed or whether it is crystalline or amorphous. The patent broadly states (p. 4) that the composition may be prepared by dissolving the drug and HPMCAS in an organic solvent, then remove the solvent by vacuum-drying, freeze-drying or spray drying. There is no further mention at all as to a spray drying method, conditions or any guidance on how spray-drying a solid dispersion would be performed, let alone how to make an amorphous spray-dried solid dispersion. As such and as further discussed in detail below, Miyajima fails to teach a spray dried solid dispersion consisting of amorphous drug molecularly dispersed in the HPMCAS. Also as discussed below and evidenced in the accompanying § 1.132 Declarations, producing a spray dried solid dispersion consisting of amorphous drug molecularly dispersed in HPMCAS is not inherently disclosed in Miyajima. Further, Miyajima fails to enable a skilled artisan how to spray dry such a solid dispersion in 1997.

Nothing in Kigoshi indicates that Kigoshi produced a spray dried solid dispersion consisting of amorphous drug molecularly dispersed in HPMCAS. There is insufficient guidance (no guidance) in Kigoshi as to spray-drying process conditions that one of ordinary skill in the art (in 1997) could use to make a spray-dried solid dispersion consisting of amorphous drug molecularly dispersed in HPMCAS. Certainly there is no guidance to test the Kigoshi disclosure to determine whether a spray-dried solid dispersion consisting of amorphous drug molecularly dispersed in HPMCAS would have resulted, at least in part because the only guidance for making the Kigoshi compositions are examples that describe a fluid bed granulator process (not spray drying).

Hikosaka provides no guidance as to spray-drying conditions or methods or any other disclosure as to how one would make a spray-dried solid dispersion consisting of amorphous drug molecularly dispersed in HPMCAS. The only method guidance, Examples 1-4, besides not being HPMCAS, do not provide any detail on spray drying conditions (nor does the disclosure in general) so reproducing what Hikosaka performed to get samples representative of the powder patterns disclosed in the patent is impossible. The Hikosaka HPMCAS examples (Examples 5 and 6) are evaporated, not spray dried. Since there is insufficient guidance (no guidance) in Hikosaka as to the spray drying process conditions to make its solid dispersion, one of ordinary skill in the art cannot test the Hikosaka disclosure to determine whether a spray-dried dispersion consisting of amorphous drug molecularly dispersed in HPMCAS could have resulted.

C. **Argument in Detail**

1. The pending claims all require a spray-dried solid dispersion consisting of a sparingly water-soluble drug and HPMCAS, the drug being molecularly dispersed and amorphous (non-crystalline) in the dispersion. In addition, the dispersion is a homogeneous solid solution of the drug in the HPMCAS.[1]

The prior art, to anticipate or make obvious the present claims, must disclose the following:

- A spray dried solid homogeneous dispersion consisting of an amorphous drug and HPMCAS;
- the drug being molecularly dispersed and consisting of amorphous drug[2] (i.e., non-crystalline drug or substantially completely amorphous) in the dispersion.

As recognized by the Examiner, none of the cited references teach or suggest a spray-dried solid dispersion consisting of an amorphous drug in the HPMCAS dispersion. The Examiner instead asserts that the references inherently disclose all–amorphous spray dried solid dispersions (Office Action dated 8/26/2011, p. 3, lines 1-3; Ev. App. 5). This is incorrect (as explained below).

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[1] The Examiner, in the Advisory Action, asserted that **there is nowhere in the applicant's specification that says spray drying produces completely amorphous dispersions."**
While there is no explicit recitation in the specification stating "consisting of" an amorphous drug dispersion such substantially completely amorphous drug dispersion is implicit in the application based on, for example, the following:

- P. 4, line 26 "The sparingly soluble drugs suitable for use in this invention can be crystalline or amorphous in their undispersed state. A crystalline drug, once dispersed, is substantially non-crystalline as determined by scanning calorimetry or x-ray diffraction."
- P. 11, lines 9-19 arguable support: "It has been determined that a spray dried solid dispersion of a sparingly-soluble drug in HPMCAS has unique properties making it broadly useful for preparing oral dosage forms. While not wishing to be bound by any particular theory or mechanism, it is believed that in order for a solid amorphous dispersion of a drug in a matrix material to function optimally in improving the bioavailability of sparingly soluble drugs, the matrix material must generally provide the following functions:
  1. disperse the drug, thereby preventing or retarding the rate of crystallization in the solid state,
  2. dissolve *in vivo,* thereby allowing the drug to be released to the gastrointestinal tract,
  3. inhibit the precipitation or crystallization of aqueous dissolved drug.
- P. 12, line 10 can infer non-crystalline from the statement: "Surprisingly, a solid amorphous dispersion comprising a spray dried mixture of HPMCAS and a sparingly soluble amorphous drug, that is, one that shows little tendency to crystallize from its amorphous state can benefit from this invention."
- P. 27, Example 4; P. 30, Example 15; P. 37 comparative examples; P. 50 Example 19 with comparative example – either state or infer that a "substantially amorphous powder" was prepared.

[2] Claim 1 uses "consisting of" language:

A spray dried solid dispersion consisting of a sparingly water-soluble drug and hydroxypropyl methylcellulose acetate succinate (HPMCAS), said drug being molecularly dispersed and amorphous in said dispersion, having a drug:polymer weight ratio between 1:0.4 and 1:20, and said dispersion is a homogeneous solid solution of said drug in said HPMCAS.

MPEP § 2111.03 states: The transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. *In re Gray*, 53 F.2d 520, 11 USPQ 255 (CCPA 1931); *Ex parte Davis*, 80 USPQ 448, 450 (Bd. App. 1948) ("consisting of" defined as "closing the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith.").

2. There is no mention whatsoever in any of the references of a spray-dried solid dispersion consisting of amorphous drug (non-crystalline drug) molecularly dispersed in a spray-dried solid HPMCAS/drug dispersion is made or could be made.

As recognized by the Examiner, none of the references even mention a solid dispersion composition: *consisting of* amorphous drug in the solid dispersion *or consisting of* amorphous drug in a spray-dried solid dispersion *or consisting of* molecularly dispersed amorphous drug in a spray-dried HPMCAS/drug solid dispersion.

3. None of the references inherently disclose spray-dried HPMCAS/drug solid dispersion consisting of amorphous drug molecularly dispersed therein.

The Examiner asserts that the cited references disclose solvents, HPMCAS, and a drug and mention the solutions can be spray-dried and thus the product these references form is inherently completely amorphous spray-dried solid dispersions (Office Action dated 8/26/2011, p. 3, lines 1-3). This is incorrect.

a. To establish inherency the result must *necessarily* be so.

b. The Newman § 1.132 Declaration (Ev. App. 2) and evidence therein confirm that spray drying even the same solutions does *not* necessarily produce a substantially completely amorphous solid dispersion - different spray-drying process conditions produce crystalline, amorphous or a mixture of crystalline and amorphous solid dispersions depending on the process conditions used.

c. Because the process conditions for spray drying must be carefully determined to make a substantially completely amorphous solid dispersion, the Examiner's assertion that the references necessarily (i.e., inherently) disclose completely amorphous spray-dried solid solutions is improper and neither anticipation nor a *prima facie* case of obviousness of the claims have been proven.

4. The cited references do not disclose any spray-drying process conditions so there is no way to practice the references' spray-drying disclosures to produce a spray-dried solid dispersion to determine the crystallinity of the references' solid dispersions. Appellant demonstrates that the cited references do not enable spray drying such amorphous solid dispersions (Beyerinck § 1.132 Declaration; Ev. App. 3).

a. Not a single reference cited provides any direction or guidance whatsoever as to how to perform a spray drying process.

b. The Examiner asserts that the PTO has no laboratories so cannot practice the reference's disclosures to determine if the suggested spray-dried products would consist of amorphous drug

(Office Action p. 12). However, because none of the references provide any disclosure as to the conditions and parameters for a spray-drying process, there is no way Appellant could test such disclosures–there are no disclosures of a spray-drying process to test.

c. As shown in the Beyerinck § 1.132 Declaration, many parameters of spray drying processes will affect whether the resulting HPMCAS/drug spray-dried dispersion consisting of amorphous drug in a HPMCAS solid dispersion. Besides listing such process parameters that need to be known to produce a HPMCAS/drug spray-dried molecularly dispersed and substantially completely amorphous solid dispersion in the Beyerinck § 1.132 Declaration, which determination of required extensive R&D, the Declarant also evidences how little was known as to spray-drying solid dispersions consisting of amorphous drug molecularly dispersed in HPMCAS solid dispersions at all, in 1997. Although it is nearly impossible to prove an absence of technology (it is self-evident that proving a negative is inherently problematic if not impossible), both the Beyerinck and Newman Declarants discuss evidence such as the Chidavaenzi article that illustrate how little was known about spray drying substantially completely amorphous solid dispersions in 1997, let alone nothing being known as to how to make a spray dried HPMCAS/drug molecularly dispersed and only amorphous drug in the HPMCAS solid dispersion.

5. Appellant's specification provides detailed guidance as to spray-drying process conditions that could be used to produce a substantially completely amorphous drug molecularly dispersed in a spray-dried solid HPMCAS/drug dispersion.

a. Both § 1.132 Declarations (Ev. App. 2 and 3) indicate that those Declarants believe that the present application has sufficient direction, guidance and examples in the specification such that one of ordinary skill in the art in August of 1997 could have made a spray-dried solid dispersion consisting of a sparingly water-soluble drug and HPMCAS, the drug being molecularly dispersed and amorphous in the dispersion, having a drug:polymer weight ratio between 1:0.4 and 1:20, and the dispersion being a homogeneous solid solution of said drug in the HPMCAS with little or no experimentation, through reading Appellant's disclosure.[3]

b. There is particular guidance for making the claimed solid dispersions in the specification at, for example, p. 15, lines 16-19, p. 15, line 25 to p. 16, line 26, p. 21, line 23 to p. 24, line 9 and examples 15, 23, 1, 25, 26, 28 and 30.

c. The Examiner asserts that Appellant has not provided a list of solvents and conditions suitable for making the claimed solid dispersions (Office Action dated 8/26/2011, p. 12). This is incorrect as

[3] It is noted that the Examiner asserted, in the Advisory Action, that the claims have not recited conditions necessary for a substantially completely amorphous solid dispersion. The composition claims do not need to recite the method of making conditions as long as the specification is enabling to make the claimed compositions. The Beyerinck and Newman § 1.132 Declarations include paragraphs listing where in the specification sufficient spray drying guidance is provided to produce the claimed dispersions.

evidenced by the § 1.132 Declarations, Appellant's specification (see paragraph b. above), and as shown in particular the description of solvents in the present specification at p. 17, line 3-17.

6. Appellant demonstrates that developing spray drying processes to make a substantially completely amorphous drug molecularly dispersed in a spray-dried solid HPMCAS/drug dispersion was much more than routine experimentation and the asserted references are not enabling for making such solid dispersions.

Appellant presented evidence that the references fail to enable one of ordinary skill in the art to make spray-dried solid dispersions of a drug and HPMCAS wherein the drug is molecularly dispersed in the dispersion (claim 1), the drug is substantially completely amorphous (i.e. "consists of ... amorphous drug") in the dispersion (claim 1), the drug is homogeneous in the dispersion (claim 1), and the drug is a solid solution in HPMCAS (claim 1). Appellant also presented evidence that producing the claimed solid dispersions was much more than mere experimentation (see the Beyerinck § 1.132 Declaration, Ev. App. 3, and the information below).

Appellant notes that the Examiner asserted Appellant had not shown Miyajima, Kigoshi and Hikosaka drugs and HPMCAS could not be dissolved in a common solvent (Office Action dated 8/26/2011, p. 11). Appellant respectfully asserts that this is not relevant to the present issue as it is not the ability to dissolve the drugs in a common solvent that is lacking in these references but instead it is the complete failure of these references to disclose a spray-dried HPMCAS/amorphous drug molecularly dispersed or to disclose how to spray dry such a solid dispersion. The references are not enabling as to making the claimed spray-dried solid dispersions - naming of a product without enabling one of ordinary skill in the art as to how to make the product is insufficient to support rejections of the claims.

The Law of Enablement in Regard to Prior Art References

In order to act as anticipating prior art, a reference (or combination of references) must enable one of ordinary skill in the art to make the invention without undue experimentation (at the time of the invention). *Impax Laboratories Inc. v. Aventis Pharmaceuticals Inc.*, 545 F.3d 1312 (Fed. Cir. 2008). In other words, the prior art must inform as to how to make the claimed invention. *Minn. Mining & Mfg. Co. v. Chemque, Inc.*, 303 F.3d 1294, 1301 (Fed. Cir. 2002) (Authority Appendix 1).

The naming of a spray-dried composition in a reference, without more, cannot constitute a teaching disclosure of the spray dried composition and the reference is not enabling prior art. One of ordinary skill in the art must be able to make or synthesize the composition for the reference to be considered enabling prior art for the teaching of the composition. *In re Hoeksema*, 399 F.2d 269 (CCPA 1968) (Auth. App. 2). In *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009) (Auth. App. 3) the court further confirmed the court's holding in *In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988) (Auth. App. 4), as reinvigorated by the Supreme Court in *KSR* (*KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727 (2007) (Auth. App. 5), that the cited references must contain "detailed enabling methodology

for practicing the claimed invention, a suggestion to modify the prior art to practice the claimed invention, and evidence suggesting that it would be successful." (Emphasis added.)

Specifics Regarding the Lack of Enablement of the Miyajima, Kigoshi and Hikosaka References for that which they are Cited

The Miyajima, Kigoshi and Hikosaka references all simply in passing mention that compositions might be spray dried, but none offer any guidance in test or in any of the examples for making spray-dried solid dispersions consisting of amorphous drug molecularly dispersed in a HPMCAS/drug solid dispersion.

i. As discussed above and in the record of this application, each of these references makes only a passing mention of spray drying and provides nothing more. None of the references give any guidance, let alone sufficient detail, for one of ordinary skill in the art to make the spray dried solid dispersion claimed by Appellant in 1997.

ii. The references do not provide sufficient information necessary to make the claimed spray-dried dispersions, which require HPMCAS/drug-solution droplets be sufficiently dry enough by the time they reach a wall of a suitable spray-drying apparatus that they are essentially solid, so that they form a fine powder and do not stick to the apparatus wall, or so that the spray dried dispersion is a homogeneous solid solution with the drug being molecularly dispersed and amorphous therein. See the Beyerinck § 1.132 Declaration (Ev. App. 3) for discussion in this regard.

iii. As discussed above and in the record of this application, none of the references teach how to make or enable making of a spray dried solid dispersion where the drug is substantially completely amorphous in the dispersion.

No spray drying process parameters, guidance or even suggestion of the same are provided in any of the cited references and determination of the same would require undue experimentation.

Appellant understands that a further test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that the cited references satisfy the enablement requirement and whether the complex and necessary extensive experimentation is "undue."

In *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) (Auth. App. 6), the Court indicated that the factors to be considered when determining whether experimentation is undue include but are not limited to:

(i) The breadth of the claims;
(ii) The nature of the invention;
(iii) The state of the prior art;
(iv) The level of one of ordinary skill;
(v) The level of predictability in the art;
(vi) The amount of direction provided in the disclosure;
(vii) The existence of working examples in the disclosure; and
(viii) The quantity of experimentation needed to make the compositions based on direction provided in the disclosure.

Evidence that the Miyajima, Kigoshi and Hikosaka References are Non-Enabling to Make the Claimed Spray Dried Dispersions - the Mere Mention of the term "Spray Drying" being Insufficient to Provide the Necessary Guidance and Experimentation Necessary to do the Same Would Be Undue

Based on all of the *Wands* factors, Miyajima, Kigoshi and Hikosaka are not enabling (see the Beyerinck and Newman § 1.132 Declarations; Ev. App. 2 and 3) and any experimentation in attempt to make the claimed spray-dried compositions would be undue under the law.

(i) The breadth of the claims – Miyajima, Kigoshi and Hikosaka do not teach or suggest how to make the claimed spray dried dispersions.

(ii) The nature of the invention – none of Miyajima, Kigoshi and Hikosaka is directed to spray dried dispersions.

(iii) The state of the prior art – the prior art of record does not teach or suggest how to make the claimed spray dried dispersions; nothing provides even a hint of guidance as to any of the necessary information as set forth above. Importantly, the application priority goes back to 1997, at the very infancy of such pharmaceutical spray-drying techniques.

(iv) The level of one of ordinary skill – the level of skill is that of a chemist or chemical engineer or physicist with a Bachelors of Science or higher degree. See, for example, the Beyerinck § 1.132 Declaration.

(v) The level of predictability in the art – the level of predictability in the art is low, as the predictability of chemistry in general is low, especially in light of the fact that there is a multitude of parameters, components and other such factors required to produce a suitable spray dried dispersion composition as claimed. Again, please see the Beyerinck and Newman § 1.132 Declarations.

(vi) The amount of direction provided by the disclosure – there is no direction provided in any of the references cited as how to make the claimed spray dried dispersion compositions or any spray dried composition at all. The Examiner provides no evidence whatsoever in the cited references or otherwise as to an enabling prior art disclosure.

(vii) The existence of working examples – there are no examples in the cited references showing or describing how to make the claimed spray-dried dispersion compositions.

(viii) The quantity of experimentation needed based on the content of the references – spray-dried dispersions require methods having a complex set of parameters, conditions and methodologies. Varying all these different parameters, conditions and methodologies, to make the claimed spray-dried dispersion compositions with the desired physical characteristics, considering it from the standpoint of simple mathematics, *per se* illustrates the extensive quantity of experimentation that was required for the inventors to develop the disclosed invention. (See the Beyerinck and Newman § 1.132 Declarations.)

Weighing the eight factors above, it is a fair conclusion that the cited references require undue experimentation and, thus, are not enabling for making a spray-dried dispersion consisting of a sparingly water-soluble amorphous drug molecularly dispersed in HPMCAS, having a drug:polymer weight ratio between 1:0.4 and 1:20, and said dispersion is a homogeneous solid solution of said drug in said HPMCAS.

Specific Claim Rejection Responses - 35 U.S.C. § 102

Claims 1, 4, 23, 49-51, 53-56 and 5-8 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Miyajima et al. (EP 0 344 603).

Miyajima fails to teach a spray dried HPMCAS/drug molecularly dispersed and substantially completely amorphous solid dispersion. As shown above, producing a substantially completely amorphous solid dispersion of HPMCAS/drug combination is not inherently disclosed in Miyajima. Further, Miyajima fails to disclose how to spray dry such a solid dispersion and as such, cannot be tested nor considered as anticipatory prior art for a spray-dried solid dispersion consisting of an amorphous drug molecularly dispersed in a HPMCAS/drug solid dispersion.

Appellant respectfully requests this rejection be reversed.

Claims 1, 4, 49-51 and 53-56 are rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Kigoshi et al. (EP 0 784 974).

Kigoshi fails to teach a spray dried HPMCAS/drug molecularly dispersed and substantially completely amorphous solid dispersion. As shown above, producing a substantially completely amorphous solid dispersion of HPMCAS/drug combination is not inherently disclosed in Kigoshi. Further, Kigoshi fails to disclose how to spray dry such a solid dispersion and as such, cannot be tested nor considered as anticipatory prior art for a spray-dried solid dispersion consisting of an amorphous drug molecularly dispersed in a HPMCAS/drug solid dispersion.

Appellant respectfully requests reversal of this rejection.

Claims 1, 4, 49, 53, 54, 55, 56 and 58 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hikosaka (JP 57-176907).

Hikosaka fails to teach a spray dried HPMCAS/drug molecularly dispersed and substantially completely amorphous solid dispersion. As shown above, Hikosaka fails to disclose how to make a spray-dried solid dispersion consisting of an amorphous drug molecularly dispersed in a HPMCAS/drug solid dispersion and as such, cannot be tested nor considered as prior art for such.

Appellant respectfully requests reversal of the rejection.

35 U.S.C. § 103

Claims 1, 23, 50 and 51 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Miyajima et al. (EP 0 344 603) or Kigoshi et al. (EP 0 784 974).

Because neither reference teaches a spray-dried solid dispersion consisting of amorphous drug molecularly dispersed in a HPMCAS/drug solid dispersion, the combination of the references does not teach or suggest the claimed solid dispersions. As shown, producing such a substantially completely amorphous solid dispersion of HPMCAS/drug combination is not inherently disclosed in either reference. Further, the references fail to disclose how to spray dry such a solid dispersion and as such, cannot be tested nor considered as prior art for the same.

Appellant respectfully requests reversal of the rejection.

Claims 1, 4, 36, 37, 49-51 and 53-56 rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kigoshi et al. (EP 0 784 974) in view of Madhusoodanan et al. ("Efficacy of risperidone treatment for psychoses associated with schizophrenia, schizoaffective disorder, bipolar disorder, or senile dementia in 11 geriatric patients: a case series," in J. Clin. Psychiatry, 1995 Nov:56(11):514-8) and further in view of Bymaster et al. (6,147,072).

Because none of these references teach a spray-dried solid dispersion consisting of amorphous drug molecularly dispersed in a HPMCAS/drug solid dispersion, the combination of the references does not teach or suggest the claimed solid dispersions. As shown, producing such a substantially completely amorphous solid dispersion of HPMCAS/drug combination is not inherently disclosed in the primary reference and the Examiner does not assert that the other references disclose such (since they do not). Further, the references fail to disclose how to spray dry such a solid dispersion and as such, cannot be tested nor considered as prior art for the same.

Appellant respectfully requests reversal of the rejection.

While the Examiner has required that Appellant prove the prior art does not produce a substantially completely amorphous spray-dried dispersion as claimed, since the cited art merely mentions the words spray drying but provide no guidance on how it would be performed, Appellant cannot test the cited art's non-existent spray drying methods to show that the non-existent methods do not make spray-dried solid dispersion consisting of amorphous drug molecularly dispersed in HPMCAS.

Reversal of all rejections is respectfully requested.

Respectfully submitted,

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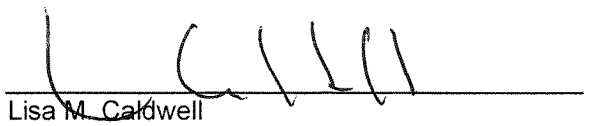
By 

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CLAIMS APPENDIX

1. (Rejected) A spray dried solid dispersion consisting of a sparingly water-soluble drug and hydroxypropyl methylcellulose acetate succinate (HPMCAS), said drug being molecularly dispersed and amorphous in said dispersion, having a drug:polymer weight ratio between 1:0.4 and 1:20, and said dispersion is a homogeneous solid solution of said drug in said HPMCAS.

2. - 3. (Canceled)

4. (Rejected) The spray dried solid dispersion of claim 1, wherein said drug is amorphous when undispersed.

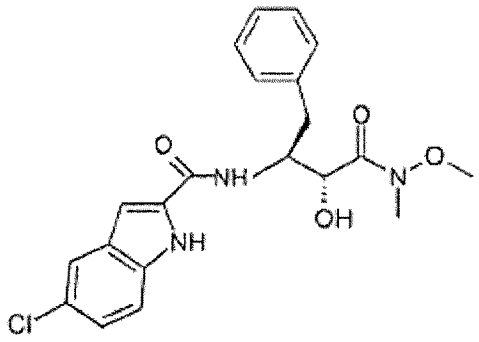
5. - 22. (Canceled)

23. (Rejected) The spray dried solid dispersion of claim 1, in the form of particles less than 100 μm in diameter.

24. - 27. (Canceled)

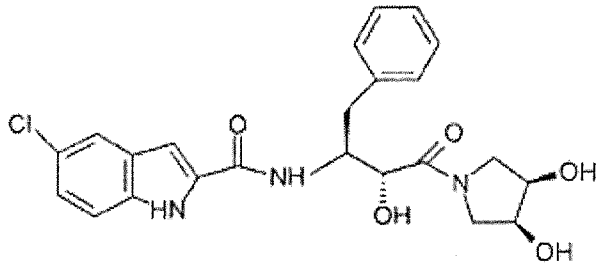
28. (Withdrawn) A composition as defined in claims 1 and 15 wherein said drug is a glycogen phosphorylase inhibitor.

29. (Withdrawn) A composition as defined in claims 1 and 15 wherein said drug is



or a pharmaceutically acceptable salt thereof.

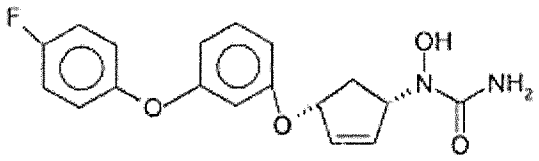
30. (Withdrawn) A composition as defined in claims 1 and 15 wherein said drug is



or a pharmaceutically acceptable salt thereof.

31. (Withdrawn) A composition as defined in claims 1 and 15 wherein said drug is a 5-lipoxygenase inhibitor.

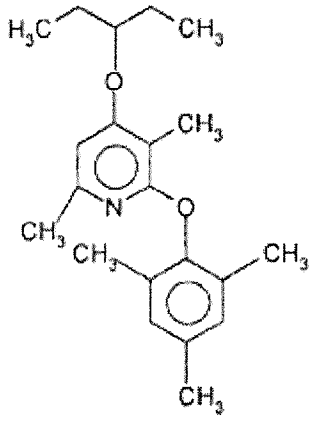
32. (Withdrawn) A composition as defined in claims 1 and 15 wherein said drug is



or a pharmaceutically acceptable salt thereof.

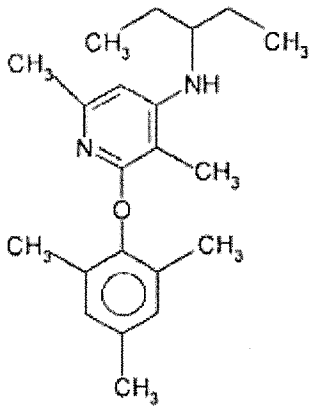
33. (Withdrawn) A composition defined in claims 1 and 15 wherein said drug is a corticotropic releasing hormone (CRH) inhibitor.

34. (Withdrawn) A composition as defined in claims 1 and 15 wherein said drug is



or a pharmaceutically acceptable salt thereof.

35. (Withdrawn) A composition as defined in claims 1 and 15 wherein said drug is



or a pharmaceutically acceptable salt thereof.

36. (Rejected) The spray dried solid dispersion of claim 1, wherein said drug is an antipsychotic.

37. (Rejected) The spray dried solid dispersion of claim 1, wherein said drug is ziprasidone.

38. (Withdrawn) A composition as defined in claims 1 and 15 wherein said drug is selected from griseofulvin, nifedipine, and phenytoin.

39. - 48. (Canceled)

49. (Rejected) The spray dried solid dispersion of claim 1, wherein said dispersion comprises spray dried particles that are solidified in less than 2 seconds.

50. (Rejected) The spray dried solid dispersion of claim 1, in the form of particles having a residual solvent content less than 2 wt%.

51. (Rejected) The spray dried solid dispersion of claim 1, in the form of spray dried particles from a solution in which the concentration of drug in the solvent is less than 20 g/100 g and in which the total solids content is less than 25 weight%.

52. (Canceled)

53. (Rejected) The spray dried solid dispersion of claim 1, wherein said drug has a dose to aqueous solubility ratio greater than 100.

54. (Rejected) The spray dried solid dispersion of claim 1, wherein said drug is crystalline when undispersed.

55. (Rejected) The spray dried solid dispersion of claim 1, having a drug:polymer weight ratio between 1:0.5 and 1:20.

56. (Rejected) The spray dried solid dispersion of claim 1, having a drug:polymer weight ratio between 1:1 and 1:20.

57. (Withdrawn) The spray dried solid dispersion of claim 1, wherein said drug is selected from the group consisting of glycogen phosphorylase inhibitors, 5-lipoxygenase inhibitors, corticotropic releasing hormone inhibitors, griseofulvin, nifedipine, and phenytoin.

58. (Rejected) The spray dried solid dispersion of claim 1, wherein said spray dried solid dispersion is supersaturated in said drug.

EVIDENCE APPENDIX INDEX

1. Prior Appeal before the Board of Patent Appeals and Interferences, Appeal No. 2010-009640; Decision, March 29, 2011.

2. Declaration of Ann W. Newman Under 37 C.F.R. § 1.132 filed November 28, 2011.

3. Declaration of Ronald A. Beyerinck Under 37 C.F.R. § 1.132 filed November 28, 2011.

4. Advisory Action dated December 22, 2011.

5. Office Action dated August 26, 2011.

AUTHORITIES CITED APPENDIX

1. *Impax Laboratories Inc. v. Aventis Pharmaceuticals Inc.*, 545 F.3d 1312 (Fed. Cir. 2008).
2. *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968).
3. *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009).
4. In re O'Farrell, 853 F.2d 894 (Fed. Cir. 1988).
5. *KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727 (2007).
6. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988).

RELATED PROCEEDINGS APPENDIX

Prior Appeal before the Board of Patent Appeals and Interferences, Appeal No. 2010-009640; Decision, March 29, 2011 (Evidence Appendix 1).